DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

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APR 19 2000

Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

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By Certified Mail - Return Receipt Requested

Warning Letter

N. Franklin Adkinson, Jr., M.D.
Johns Hopkins Asthma & Allergy Center
Clinical Immunology Unit Office #2
5501 Hopkins Bayview circle
Baltimore, Maryland 21224-6821

Dear Dr. Adkinson:

During the period of January 27 to February 22, 2000, Mr. David Glasgow, an investigator from the Food and Drug Administration (FDA) FDA Baltimore District Office, visited the Johns Hopkins Bayview Medical Center Institutional Review Board (IRB) and reviewed the records of clinical studies conducted under your supervision.

Mr. Glasgow's review documented that your activities are in violation of Section 505(i) of the Federal Food, Drug, and Cosmetic Act (the Act), and are deviations from applicable federal regulations as published in Title 21, Code of Federal Regulations, Part 312 [21 CFR 312]. The deviations include the following:

1. **You violated the clinical hold of Investigational New Drug Application (IND) — [21 CFR § 312.42(a)].**

   You submitted IND — to FDA in August of 1998, for the use of an

   —— . FDA notified you by telephone on September 18, 1998, that the IND was placed on clinical hold due to safety concerns, and instructed that you were not permitted to initiate clinical trials under the IND until the identified product safety and study protocol concerns were satisfactorily addressed. The telephone conversation was followed by a letter dated September 28, 1998, outlining the clinical hold issues. Your October 12, 1998, response to the clinical hold did not satisfactorily address FDA's concerns and, as indicated in the telephone conversation of October 30, 1998, and FDA's letter dated November 4, 1998, this IND remains on clinical hold.

   You submitted annual reports to the IRB showing that you exposed human subjects to investigational ——— after you were notified of the clinical hold.

A. ***#AAC96-10-18-02.*** Your annual report dated October 8, 1999, states that you enrolled at least 20 subjects since the previous annual report you submitted on October 8, 1998, after the FDA imposed the clinical hold.

B. ***#AAC97-10-03-01.*** Your annual report dated October 8, 1999, states that six (6) subjects had been included in the study since it began, and that four (4) had been included since the previous annual review held on December 7, 1998. In addition, in the annual report to the IRB dated October 8, 1998, you entered the box labeled "Projected Date of Study Completion" as "ongoing," just three weeks after FDA notified you of the clinical hold.

C. ***#AAC99-08-26-03.*** The IRB approved the study on October 18, 1999. Any use of the ——— after September 18, 1998, is a violation of the clinical hold.

2. **You diverted an investigational ——— for use outside of a sponsor-approved study. [21 CFR §§ 312.20(b), 312.40(d), 312.50].**

You used an investigational ——— in a manner (repeated ———) and for a purpose (———) not approved by the sponsor. According to documents you submitted to the IRB, you supervised the administration of the investigational ——— to subjects in studies #AAC96-10-18-02 and #AAC97-10-03-01, and plan to enroll subjects in study #AAC99-08-26-03.

3. **You provided misleading information to the IRB regarding the IND status of proposed research studies. [21 CFR § 312.66].**

#AAC97-10-03-01 and #AAC99-08-26-03. The initial Research Project Notifications for these studies state that the studies will be conducted under IND ——. As stated in item 2, above, the sponsor did not approve the use of the investigational ——— for immunotherapy research.

4. **You failed to obtain informed consent in accordance with the provisions of 21 CFR Part 50. [21 CFR Part 50 and § 312.60].**

Each of the informed consent documents you prepared for the studies listed in item 1, above, state the following: "..Under certain conditions, people responsible for making sure that the research is done properly may review your study records. This might include people from...the Food and Drug Administration...." This statement is misleading to potential study subjects since it implies that FDA has allowed the research to be conducted, when, in fact, the study was conducted in violation of a clinical hold imposed by FDA.

You should immediately cease administering the investigational ——— to human subjects outside of sponsor-approved protocols, and immediately discontinue use of the ——— until the clinical hold issues are satisfactorily resolved. Failure to do so may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to disqualification.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational drugs. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

Please notify this office in writing, within fifteen (15) business days of receipt of this letter, of the actions you have taken to correct these violations. Any plans of action must include projected completion dates for each action to be accomplished.

If you have questions or comments about the contents of this letter, you may contact Patricia Holobaugh, Consumer Safety Officer, Bioresearch Monitoring, Division of Inspections and Surveillance, at (301) 827-6347.

Your written response should be addressed to:

Ms. Patricia Holobaugh (HFM-650)
Division of Inspections and Surveillance
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448
Telephone: (301) 827-6347

Sincerely,

Steven A. Masiello
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation
and Research